Dietary fat intake is associated with hepatobiliary cancers which carry a poor prognosis causing over 20,000 deaths per year in the US alone. We hypothesized that excess lipid accumulation in the liver promotes hepatic cancer through inflammation and oxidative DNA damage. In order for eukaryotic cells to protect genomic integrity, the protein kinase ataxia telangiectasia mutated (ATM) responds to oxidative DNA damage and DNA strand breaks. Failure to activate ATM following damage leads to defective cell cycle control and impaired DNA repair. In this study, ATM knockout mice were used as a sensitized background to assess the effects of oxidative stress and DNA damage associated with hepatosteatosis. ATM-deficient and control mice were fed a high fat diet for eight weeks, and then liver tissue was analyzed for apoptosis. It was expected that more apoptotic cells would be found in ATM-deficient mice fed the high fat diet than in control mice due to DNA break repair deficiencies. Liver tissues were sectioned and stained by TUNEL assay, a method for detecting DNA fragmentation that occurs during apoptosis. The TUNEL immunohistochemistry protocol was first optimized for hepatocytes. Positive cells were counted in multiple 40X fields from each tissue section. Statistical differences between groups were determined by comparison of the fraction of positive cells. There were more apoptotic cells in livers from mice fed a high fat diet relative to those fed the normal diet. Interestingly, among mice fed the high fat diet there was a slight decrease in apoptosis in ATM deficient mice relative to controls. Although this difference did not reach statistical significance, this may indicate that ATM is required for inducing hepatic apoptosis in response to stresses associated with increased dietary fat consumption. Additional staining for cell proliferation as well as DNA damage response activation will be performed in the future. This study will begin to elucidate the interaction between lipid metabolism, oxidative stress, DNA damage and hepatobiliary oncogenesis and will establish a new mouse model that will provide a powerful tool for future mechanistic and translation studies of hepatobiliary disease.